

REMARKS

Election of Species

In response to the Election/Restriction mailed 5 December 2001, and the requirement for an election of species therein, applicants elected the species of Example 1 disclosed on page 182 of the specification which corresponds to the first compound of claim 8. Following Applicants identification of an individual species the guidelines of MPEP 803.02 must be followed. Instead, the Examiner, based on Applicants' election of species set forth a definition of the scope of compounds to be examined in terms of a restriction requirement.

The Examiner initially presented an Election of Species Requirement, to which the Applicants fully responded by election of a species. In the Office Action of [insert] the election was referred to as a Restriction. Applicants' respectfully submit that it was improper to change the characterization of the requirement after the election was made. Applicants' consider the requirement as an Election of Species under Markush practice.

Request to Withdraw Finality

At page 4, paragraph 5 of the Office Action, the Examiner alleges that claim 32 is newly added and necessitated the new ground of rejection. This is not correct. Claim 32 was previously presented for Examination in the amendment filed 8 July 2005. As such the Examiner has introduced a new grounds for rejection that was not necessitated by Applicant's amendments. Thus, it is respectfully urged that the finality of the Office Action be withdrawn.

Rejections under 35 USC §112, first paragraph

Claims 1-2, 5-6, 9-12 and 31 stand rejected under 35 U.S.C. §112. The rejection is respectfully traversed.

Applicant request clarification with regards to the objection to the recitation of "one of R¹⁰ and R¹¹ is H, and the other is 2-Methyl-4-thiazoyl" since this recitation is no longer present in the claims.

Only claims 2 and 5 previously contained the recitation "one of R¹⁰ and R¹¹ is H, and the other is 2-Methyl-4-thiazoyl" and in the previous amendment, at the Examiners

suggestion, the limitation was removed and claims 2 and 5 were made independent claims depicting the structural formula of naturally occurring epothilone A or B along with the original variables presented in claims 2 and 5. The specification provides ample support for the amendment and a "generic description" thereof since the originally presented claims 2 and 5 recited the phrase "the remainder of the molecule is identical to naturally occurring epothilone A or B" and the first paragraph of the specification provides a structure and reference to naturally occurring epothilone A and B. The naturally occurring formula shown on page 1 clearly shows the 2-methyl-4-thiazolyl structure. The subgenus, as currently claimed, with this moiety finds support in original claims 2 and 5.

Applicants' note that the Examiner is trying to get Applicants' to narrow their invention to a more limited subgenus by calling an election of species requirement a Restriction. Yet the Examiner would apparently disallow claiming such a more limited subgenus because it was not originally specifically described in that scope. Applicants' find this practice inconsistent. In any event, the scope of the current claims is specifically described in the disclosure.

Thus, the rejection should be withdrawn, particularly since none of the claims contain the objected to recitation "one of R¹⁰ and R¹¹ is H, and the other is 2-Methyl-2-thiazoyl."

Double Patenting Rejection

As to the Double Patenting rejection, although the Examiner does not mention the 09/913,163 application in this rejection, Applicants' assume that the Examiner is possibly referring to allowed claims 1-5, 17-18 and 20-21 of the 09/913,163 application. It appears that the double patenting rejection in this application is withdrawn since a terminal disclaimer has already been filed in the 09/913,163 application and, thus, according to the PTO rules, one is not required here.

As to the '736 patent, the Examiner did not address the distinction pointed out in the response filed February 2006, i.e., that the claims of US 6,610,736 require the R⁸ group to be cyano or halogen. The present claims do not include compounds where R⁸ is cyano or halogen. Applicants again urge that this argument be addressed. The claims are clearly distinct from those of the '736 patent.

With regards to the 10/631,011 application which is directed to an effector conjugate that requires a structure of formula III or IV, the Examiner alleges that 10/631,011 teaches esterified pro-drugs and that pro-drug conjugates are obvious formulation of compounds for delivery purposes. Regardless of any prodrug effect, the claims do not encompass the same subject matter. Furthermore, nothing in the claims of the '011 application teaches or suggests the breaking up of the claimed conjugates to obtain the partial structures as separate compounds. Thus, the instant claims are directed to patentably distinct subject matter and are not obvious variants of the claims of the '011 application. The Examiner merely makes the conclusory statement that a pro-drug is obvious. No legal or scientific support or other reasoning is provided. Thus, no motivation to support obviousness is provided.

Withdrawal of the rejection is respectfully requested.

The Rejections Under 35 U.S.C § 103

The Examiner has maintained the §103 rejection of Claims 1-2, 5-6, 9-12 and 31 over Nicolaou et al.

At page 4, paragraph 4, the Examiner alleges that none of the tested compounds presented in the declaration of Dr. Klar contain the $-\text{CH}_2-\text{CH}_2-$ linker (D-E linker) that is present in Nicolaou's compound. This is incorrect. All of the test compounds contain $-\text{CH}_2-\text{CH}_2-$ as the D-E linker. Clarification is respectfully requested. The following comments are based upon the assumption that the Examiner is referring to the R^5 methyl that is present on the test compounds but not Nicolaou's compound. The prior art compound and the claimed invention are homologues with respect to the alkyl group at the R^{2a} and R^{2b} positions. The proviso portion of the instant claims recites "...whereby, if -D-E- stands for $-\text{CH}_2-\text{CH}_2-$ and Y stands for an oxygen atom, at least one of R^{2a} and R^{2b} is not hydrogen or methyl." Nicolaou's compound, which contains a methyl at one of R^{2a} and R^{2b} positions, is already excluded based on this proviso. The obviousness rejection set forth in the office action dated March 4, 2004 is based on the premise of homology at the R^{2a} and R^{2b} positions. Thus, Applicant's burden is to overcome the obviousness rejection based on the premise of homology at the R^{2a} and R^{2b} positions. The declaration includes test of compounds, which meet the proviso against compounds

in which-D-E- stands for $-\text{CH}_2-\text{CH}_2-$ and Y stands for an oxygen atom and at least one of R^{2a} and R^{2b} is methyl, as is the case with Nicolaou's compound.

Thus, regardless of the R^5 methyl, the declaration has demonstrated that compounds that differ by a methylene linkage at the R^{2a} and R^{2b} positions show unexpected properties. The burden of proof has been met. No further test data should be required. Such would be essentially redundant, would require the inventor to synthesize additional compounds and would seem to serve for nothing except to perhaps unduly burden the inventor. Thus, the presumption of similar properties based on homology at the R^{2a} and R^{2b} positions, which forms the basis for the rejection, is disproved and the rejection should be withdrawn.

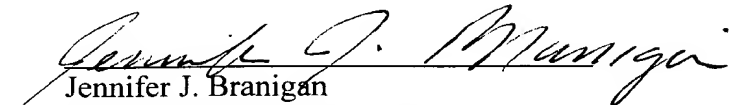
Claims 8 and 32 are rejected under 35 U.S.C §103 as being unpatentable over Danishefsky (US 6,242,469). The Examiner is relying upon the provisional application filing date of 3 December 1996 as the prior art date for the reference. However, Figure 42B (or a structure corresponding to compound 34 of Figure 42B) is not present in this earlier filed provisional application. Thus, the figure 42B disclosure does not have support in the earlier provisional application and its later disclosure, the non-provisional filing, is not prior art against the instant claims.

In any event, the rejection points to compound 34 of Figure 42B. We note that like Nicolaou et al., compound 34 of Figure 42B has a methyl at the R^{2a} and R^{2b} positions. Thus, the comparative data applies equally.

Furthermore, as stated above, the Examiner alleges that claim 32 is newly added although claim 32 was previously presented for Examination. Accordingly, Applicant's urge withdrawal of the finality of the action and a withdrawal of the rejections under 35 USC §103.

In view of the above remarks, it is respectfully submitted that the claims of the application are fully supported by the specification and as such are in order for allowance.

Respectfully submitted,


Jennifer J. Branigan
Patent Agent (Reg. No. 40,921)

John Sopp (Reg. No. 33,103)
Attorney for Applicants

MILLEN, WHITE, ZELANO & BRANIGAN, P. C.
Arlington Courthouse Plaza I
2200 Clarendon Boulevard, Suite 1400
Arlington, Virginia 22201
Direct dial: (703) 812-5305
Internet address: jbranigan@mwzb.com

Filed: **4 August 2006**

JJB:K:\Sch\1742\July 06 Reply.doc